

**RESPONSE**

**U.S. Appln. No. 09/674,377**

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application:

**LISTING OF THE CLAIMS:**

Claim 1. (Previously Presented) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor; or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence of (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF.

Claim 2. (Previously Presented) A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the

**RESPONSE**

**U.S. Appln. No. 09/674,377**

growth of vascular endothelial cells induced by bFGF and/or VEGF.

Claim 3. (Previously Presented) A neovascularization inhibitor as set forth in claim 1 or 2, wherein said polypeptide has at least one hairpin domain and 4 Kringle domains.

Claim 4. (Previously Presented) A neovascularization inhibitor as set forth in claim 1 or 2, wherein said polypeptide is one obtainable by elastase digestion of hepatocyte growth factor.

Claim 5. (Original) A neovascularization inhibitor comprising the polypeptide defined by SEQ ID NO:1 and a pharmaceutically acceptable carrier.

Claim 6. (Original) A neovascularization inhibitor comprising the polypeptide defined by SEQ ID NO:2 and a pharmaceutically acceptable carrier.

Claim 7. (Previously Presented) A prophylactic or therapeutic drug for a disease associated with abnormal angiopoiesis which comprises the polypeptide as set forth in claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 8. (Previously Presented) A prophylactic or therapeutic drug as set forth in claim 7, wherein said disease associated with abnormal angiopoiesis is selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors and wound granulation.

Claim 9. (Previously Presented) A prophylactic or therapeutic drug for a disease arising from overstimulation of

**RESPONSE**

**U.S. Appln. No. 09/674,377**

endothelial cells which comprises the polypeptide as set forth in claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 10. (Previously Presented) A prophylactic or therapeutic drug as set forth in claim 9, wherein said disease arising from overstimulation of endothelial cells is selected from the group consisting of enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claim 11. (Previously Presented) A conception-regulating drug comprising the polypeptide as set forth in claim 1 or 2, and a pharmaceutically acceptable carrier.

Claim 12. (Previously Presented) A method of inhibiting neovascularization which comprises administering to a subject a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF.

Claim 13. (Previously Presented) A method of inhibiting neovascularization which comprises administering to a subject a neovascularization inhibitor comprising the following

**RESPONSE**

**U.S. Appln. No. 09/674,377**

polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF.

Claim 14. (Previously Presented) A method for prophylaxis or therapy of a disease associated with abnormal angiopoiesis which comprises administering a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor (HGF); or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF to a subject in whom a prophylactic or therapeutic treatment for said disease is indicated.

**RESPONSE**

**U.S. Appln. No. 09/674,377**

Claim 15. (Currently Amended) A method for prophylaxis or therapy of a disease associated with abnormal ~~angiopoiesis~~ angiopoiesis which comprises administering a neovascularization inhibitor comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

- (a) a polypeptide having the amino acid sequence  
PyrGlu<sup>32</sup> ~ Val<sup>478</sup> of hepatocyte growth factor  
(HGF); or
- (b) a polypeptide having an amino acid sequence  
derived from the amino acid sequence defined in  
(a) by the deletion, substitution or addition of  
one or more amino acids, and having antagonistic  
activity against the c-Met/HGF receptor-mediated  
action of HGF and inhibitory action against the  
growth of vascular endothelial cells induced by  
bFGF and/or VEGF to a subject in whom a  
prophylactic or therapeutic treatment for said  
disease is indicated.

Claim 16. (Previously Presented) The method for prophylaxis or therapy as set forth in claim 14 or 15, wherein said disease is any disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claims 17-18. (Cancelled)

Claim 19. (Previously Presented) A polypeptide having an amino acid sequence defined by SEQ ID NO:2.

**RESPONSE**

**U.S. Appln. No. 09/674,377**

Claim 20. (Previously Presented) A pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 21. (Previously Presented) A pharmaceutical composition for prophylaxis or therapy of a solid cancer or/and cancer metastasis, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 22. (Previously Presented) A pharmaceutical composition as claimed in Claim 21, wherein cancer of solid cancer or cancer of cancer metastasis is lung cancer or mammary cancer.

Claim 23. (Previously Presented) A pharmaceutical composition effective for inhibition of tumor growth or metastasis, which comprises the polypeptide having an amino acid sequence defined in SEQ ID NO:2 as an active ingredient.

Claim 24. (Previously Presented) A pharmaceutical composition as claimed in Claim 23, wherein tumor is lung cancer or mammary cancer.

Claim 25. (Previously Presented) A pharmaceutical composition for prophylaxis or therapy of diseases arising from vascular hyperplasia or/and diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 26. (Previously Presented) A pharmaceutical composition as claimed in Claim 25, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial

**RESPONSE**

**U.S. Appln. No. 09/674,377**

angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claim 27. (Previously Presented) A pharmaceutical composition for controlling conception, which comprises the polypeptide having an amino acid sequence defined by SEQ ID NO:2 as an active ingredient.

Claim 28. (Previously Presented) A method for prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide having the amino acid sequence  
PyrGlu<sup>32</sup>~Val<sup>478</sup> of heaptocyte growth factor (HGF);  
or

(b) a polypeptide having an amino acid sequence  
derived from the amino acid sequence defined in  
(a) by the deletion, substitution or addition of  
one or more amino acids.

Claim 29. (Previously Presented) A method for prophylaxis or therapy of a solid cancer and/or cancer metastasis, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

Claim 30. (Previously Presented) A method for prophylaxis or therapy as claimed in Claim 28 or Claim 29, wherein cancer of solid cancer or cancer of cancer metastasis is lung cancer or mammary cancer.

**RESPONSE**

**U.S. Appln. No. 09/674,377**

Claim 31. (Previously Presented) A method for inhibition of tumor growth or metastasis, which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence  
PyrGlu<sup>32</sup>~Val<sup>478</sup> of heaptocyte growth factor (HGF);  
or
- (b) a polypeptide having an amino acid sequence  
derived from the amino acid sequence defined in  
(a) by the deletion, substitution or addition of  
one or more amino acids.

Claim 32. (Previously Presented) A method for inhibition of tumor growth and metastasis, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

Claim 33. (Previously Presented) A method for prophylaxis or therapy as claimed in Claim 31 or Claim 32, wherein tumor is lung cancer or mammary cancer.

Claim 34. (Previously Presented) A method for prophylaxis or therapy of diseases arising from vascular hyperplasia and/or diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence  
PyrGlu<sup>32</sup>~Val<sup>478</sup> of heaptocyte growth factor (HGF);  
or



**RESPONSE**

**U.S. Appln. No. 09/674,377**

- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or more amino acids.

Claim 35. (Previously Presented) A method for prophylaxis or therapy of diseases arising from vascular hyperplasia or/and diseases caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject a pharmaceutical composition containing the polypeptide having an amino acid sequence defined by SEQ ID NO:1 or SEQ ID NO:2.

Claim 36. (Previously Presented) A method for prophylaxis or therapy as claimed in Claim 34 or Claim 35, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claim 37. (Previously Presented) A method for controlling conception which comprises administering to a subject a pharmaceutical composition containing the following polypeptide (a) or (b):

- (a) a polypeptide having the amino acid sequence PyrGlu<sup>32</sup>~Val<sup>478</sup> of heaptocyte growth factor (HGF);  
or
- (b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in

**RESPONSE**

**U.S. Appln. No. 09/674,377**

(a) by the deletion, substitution or addition of one or more amino acids.